UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/668,749	09/23/2003	Hui Wang	10030304-1	2131

7590 05/02/2008

AGILENT TECHNOLOGIES, INC.
Legal Department, DL429
Intellectual Property Administration
P.O. Box 7599
Loveland, CO 80537-0599

EXAMINER	
CLOW, LORI A	
ART UNIT	PAPER NUMBER
1631	

MAIL DATE	DELIVERY MODE
05/02/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/668,749	WANG, HUI	
	Examiner	Art Unit	
	Lori A. Clow, Ph.D.	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 April 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4-11,13,15,18-20,36 and 37* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4-11,13,15,18-20,36 and 37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4/18/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 18 March 2008 has been entered.

Applicants' response, filed 18 March 2008, has been fully considered. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claims 1, 4-11, 13, 15, 18-20, 36, and 37 are currently pending. Claims 2, 3, 12, 14, 16, 17, and 21-35 have been cancelled.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 4-11 and 13 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. This rejection is necessitated by amendment to the claims.

In *In re Wands* (8 USPQ2d 1400 (CAFC 1988)) the CAFC considered the issue of enablement in molecular biology. The CAFC summarized eight factors to be considered in a determination of "undue experimentation". These factors include: (a) the quantity of experimentation necessary; (b) the amount of direction or guidance presented; (c) the presence or absence of working examples; (d) the nature of the invention; (e) the state of the prior art; (f) the relative skill of those in the art; (g) the predictability of the art; and (h) the breadth of the claims.

In considering the factors for the instant claims:

a) In order to practice the claimed invention one of skill in the art must be able to perform nanopore data analysis with a nanopore device by providing a sample, generating nanopore data, forming a distribution pattern, analyzing a distribution of target polynucleotide data points and determining at least one of a phosphorylation state, chemical integrity, and ratio of target polynucleotides to non-target polynucleotides. For the reasons set forth below, this represents undue experimentation.

b) and c) The specification states the following with respect to determining length diversity among polynucleotides in a sample:

In block 24, the distribution of the target and non-target polynucleotide data points is **analyzed**. As discussed above, the **analysis** typically produces a scatter plot having two clusters. In block 26, a determination is made regarding the presence of non-target polynucleotides in the sample. In particular, the presence of non-target polynucleotides in the sample can be determined by observing the data points that are outside of the cluster areas. The cluster areas should contain the data points corresponding to the target polynucleotides since the sample is composed of primarily target polynucleotides. Since polynucleotides having different lengths translocate the aperture with different duration, the target polynucleotides having the same lengths produce data points in the cluster areas, while non-target polynucleotides having a different length than the target polynucleotides produce data points outside of the cluster areas. In addition, non-target polynucleotides having the same length as the target polynucleotide produce data points outside of the cluster areas when the sequence of the non-target polynucleotide and target polynucleotide is not the same.

The specification teaches that the distribution of the non-target must also be analyzed in order that length diversity be determined. However, in claims 1 and 15, as amended, the analysis of the distribution of the non-target polynucleotide data points is optional and it is therefore uncertain as to how one of skill in the art would reasonable determine length diversity without the analysis of the non-target datapoints. Without the numbers from the non-target data, as they represent a distribution, the comparison to the target distribution is not possible and length diversity is not able to be determined.

d) The invention is drawn to methods of performing nanopore analysis. However, the claims, as amended, are not enabled for the length diversity determination step.

f) The skill of those in the art of molecular biology is high.

h) The claims are not enabled with respect to step (ii) because they are drawn to a method of determining length diversity without non-target distributions. The skilled practitioner would first turn to the instant specification for guidance to practice such methods. However, the instant specification does not provide specific guidance to practice these embodiments. As such, the skilled practitioner would turn to the prior art for such guidance, however, the prior art is silent. Finally, said practitioner would turn to trial and error experimentation. Such represents undue experimentation.

Response to Applicant's Arguments

1. Applicant argues that "claim 1 is directed to a method of performing nanopore data analysis that determines at least one of four alternatives". Applicant states that "only one of these four alternatives, determining length diversity, requires analyzing the distribution of non-target polynucleotide data points. Accordingly, the step of analyzing the distribution of non-

target polynucleotide data points is optional to the method in the sense that three of the four alternatives do not require such a step".

This is not persuasive. Claim 1 recites the step of "optionally analyzing the distribution of the non-target polynucleotide data points" **prior** to the determining at least one of the following steps of (i), (ii), (iii), or (iv). There is no requirement in step (ii), for length diversity, of actually having to perform the "analyzing" step, as it is "optional" prior to the recitation of the four alternatives. Therefore, the claim is fairly interpreted as possibly NOT performing the analysis of distribution of the non-target polynucleotide data points with respect to step (ii). The rejection is maintained.

Claim Rejections - 35 USC § 112-2nd paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 10, 11, 15, 18-20, 36, and 37 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 10 and 11 recite, "said method comprising analyzing the distribution of the non-target polynucleotide data points". It is unclear as to where in the method steps this occurs. Is this intended to be in place of the "optionally analyzing" or is this intended to pertain to step (ii) only, for example. Clarification is requested.

Claim 15, and dependent claims, recite, at step (iv), "a ratio of target polynucleotides to non-target polynucleotides in the sample, wherein the nanopore data analysis system is operative to analyze the distribution of the non-target data polynucleotides data points". It is unclear as to what the "analysis" of the distribution of non-target data polynucleotide data points has to do with the "ratio" of target to non-target? Is the analysis intended to analyze the distribution of non-target data polynucleotide data points with respect to the target data polynucleotide data points? This is not clear from the claim language. Clarification is requested.

Conclusion

No claims are allowed.

The outstanding rejections over claims 15, 18-20, 36, and 37 with respect to 112, 1st paragraph (enablement) are withdrawn in view of Applicant's arguments.

Inquiries

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR § 1.6(d)). The Central Fax Center Number is (571) 273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lori A. Clow, Ph.D., whose telephone number is (571) 272-0715. The examiner can normally be reached on Monday-Friday from 10 am to 6:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marjorie Moran can be reached on (571) 272-0720.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

May 1, 2008
/Lori A. Clow, Ph.D./
Primary Examiner, Art Unit 1631